Review

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Current implications of EEG and fNIRS as functional neuroimaging techniques for motor recovery after stroke

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Abstract: Persistent motor deficits are highly prevalent among post-stroke survivors, contributing significantly to disability. Despite the prevalence of these deficits, the precise mechanisms underlying motor recovery after stroke remain largely elusive. The exploration of motor system reorganization using functional neuroimaging techniques represents a compelling yet challenging avenue of research. Quantitative electroencephalography (qEEG) parameters, including the power ratio index, brain symmetry index, and phase synchrony index, have emerged as potential prognostic markers for overall motor recovery post-stroke. Current evidence suggests a correlation between qEEG parameters and functional motor outcomes in stroke recovery. However, accurately identifying the source activity poses a challenge, prompting the integration of EEG with other neuroimaging modalities, such as functional near-infrared spectroscopy (fNIRS). fNIRS is nowadays widely employed to investigate brain function, revealing disruptions in the functional motor network induced by stroke. Combining these two methods, referred to as integrated fNIRS-EEG, neural activity and hemodynamics signals can be pooled out and offer new types of neurovascular coupling-related features, which may be more accurate than the individual modality alone. By harnessing integrated fNIRS-EEG source localization, brain connectivity analysis could be applied to characterize cortical reorganization associated with stroke, providing valuable insights into the assessment and treatment of post-stroke motor recovery.

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Introduction

Stroke, a highly prevalent cerebrovascular disease, frequently leads to profound motor deficits and long-term rehabilitation challenges. With an estimated 80.1 million current survivors and 13.7 million new cases annually, stroke is a major contributor to chronic disability [1]. Nearly half of all survivors continue to experience residual motor and/or cognitive impairments even six months after stroke onset [2]. These functional impairments can manifest as limitations in activities of daily living, imposing substantial economic burdens on the individual, family, society, and healthcare system.

After stroke, motor function recovery is one of the important goals of rehabilitation treatment. While traditional rehabilitation strategies demonstrably improve motor function recovery, substantial heterogeneity exists, and their efficacy diminishes in the chronic phase. Complete functional restoration occurs in less than 15 % of patients [3]. A key potential explanation lies in the largely unclarified underlying mechanisms. Consequently, a critical need exists to personalize treatment based on individual patient characteristics. This necessitates a comprehensive understanding of individual brain network properties, alongside the identification of objective parameters capable of measuring and predicting post-stroke recovery. Such knowledge would facilitate the development of individually tailored rehabilitation plans and enable the smooth integration of modern approaches, such as non-invasive brain stimulation, virtual reality, and robotic rehabilitation, into standard patient care programs.

Stroke's functional assessment primarily relies on established clinical scales. While these scales offer practicality, affordability, and ease of administration, with limitations in objectivity, sensitivity, and reliability. Mounting evidence indicates stroke as a brain network disorder, emphasizing the dynamic nature of functional recovery beyond localized cortical changes [4, 5]. Functional reorganization and neuroplasticity, which are crucial for post-stroke recovery, extend beyond specific areas of the cortex and are intricately linked to the reshaping of brain network structure [4]. In recent decades, neuroimaging techniques, including functional magnetic resonance imaging (fMRI), positron emission tomography (PET), electroencephalogram (EEG), and functional near infrared spectroscopy (fNIRS) have emerged as powerful tools for investigating the dynamic alteration of cortical excitability and connectivity after stroke. These methods, particularly multimodal approaches, hold significant promise for enhancing the prognostication and diagnosis of motor function deficits after stroke.

fMRI and PET are two powerful tools in neuroscience, both relying on the principle of neurovascular coupling [6], which posits an inseparable link between neuronal activity, oxygen consumption, and cerebral blood flow. Increased neuronal activity in a brain region is invariably accompanied by a corresponding rise in local blood flow and oxygenation. Consequently, both fMRI and PET offer means to assess hemodynamic responses, which closely map onto neural activity within the brain. PET necessitates the injection of radiolabeled ligands, making it significantly more expensive and limiting its repeated use within the same patient. fMRI measures the blood-oxygen-level-dependent (BOLD) contrast within brain structures, providing an indirect yet informative measure of coordinated neural activity and oxygen consumption [7]. From the perspective of hemodynamic changes, fMRI excels in elucidating brain function at the macrovascular level [8]. This makes it particularly advantageous for evaluating functional states and network alterations following stroke. However, the major limitation of fMRI lies in its inapplicability in certain clinical settings involving dynamic scenarios like walking or exercise. PET necessitates the injection of radiolabeled ligands, making it significantly more expensive and limiting its repeated use within the same patient.

Different from fMRI, EEG and fNIRS are potentially appropriate for long-term subject monitoring. Previous studies have shown that fNIRS has good temporal resolution and is comparable to fMRI in physiological monitoring [9]. Importantly, compared to fMRI, fNIRS is more portable, more resistant to motion artifacts, and can be used to detect and dynamically monitor brain network recovery during rehabilitation. In contrast to fMRI, EEG has the advantages of low cost and high temporal resolution. The applications of EEG, fNIRS, and multimodal studies using EEG and fNIRS simultaneously to assess electrical and hemodynamic activity for motor recovery after stroke have increased significantly.

EEG in motor function assessment and rehabilitation after stroke

In the brain, neurons are known to communicate with each other through electrical signals, which propagate through neurites (axons and dendrites) in the neural network. EEG employs strategically placed electrodes on the scalp to detect these voltage fluctuations (Figure 1). While structural imaging methods like fMRI and PET offer superior spatial resolution, EEG excels in capturing the lightning-fast dynamics of brain currents with millisecond precision. This data, encompassing signal frequency, intensity, morphology, synchrony, and periodicity, unlocks the secrets of electrical activity across the entire cerebral cortex [10]. Owing to its non-invasive nature, exceptional temporal resolution, ease of setup, and cost-effectiveness, EEG emerges as a potent tool for longitudinal assessment of motor function in the aftermath of stroke.

EEG analysis can be broadly categorized into qualitative and quantitative approaches. During quantitative EEG (qEEG), raw EEG data undergoes computerized processing using various algorithms to convert it into the discrete frequency domain. This transformed data facilitates further analysis and comparison. Power spectrum density, symmetry indexes and connectivity metrics are the commonly used parameters of qEEG to study the association between brain activity and behavioral recovery after stroke (Figure 1).

Parameters of qEEG

Power spectrum density (PSD) and power ratio index (PRI)

To understand the correlation of motor-related neurological activity with the corresponding EEG recording, one common approach to analyze these signals is to convert them to a frequency domain. This approach transforms the continuous EEG signal into a spectrum, revealing the power spectral density (PSD) essentially, the strength of the signal at different frequencies (Figure 1). The EEG signals differentiated by the wavelength and frequency may help to detect the problems associated with the function. Delta waves (0.5–4.0 Hz), often associate with slow, deep sleep, might appear focally with subcortical lesions or more diffusely in conditions like metabolic encephalopathy. Theta waves (4–7 Hz), linked to memory and emotional processing, can shed light on cognitive functioning. Alpha waves (8–12 Hz) are the major rhythm seen in normal relaxed adults. It indicates relaxed wakefulness and disappears when opening the eyes

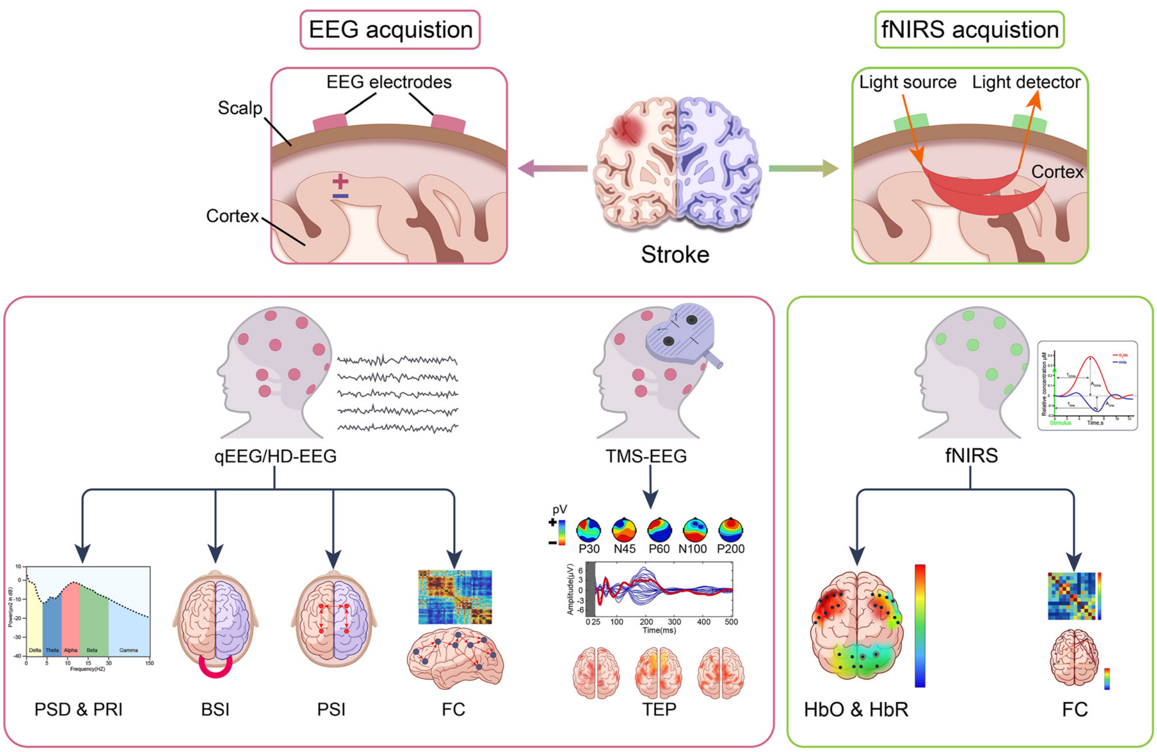

Figure 1: An overview of the EEG and fNIRS parameters commonly employed in the assessment of motor recovery after stroke. Through the electrodes attached to the scalp, EEG mainly detects the voltage fluctuations in the cortex. The parameters of qEEG and HD-EEG used for motor recovery after stroke encompass PSD and PRI, BSI and PSI, as well as FC. TMS-EEG involves the application of a single TMS pulse to the M1, whereby the combined EEG records the TEP (P30-N45-P60-N100-P200). The data recorded from the Cz electrode is represented by the red line, while the blue lines show data from all channels. FNIRS measures HbO and HbR levels, as well as FC, by the optodes positioned across various regions of the scalp during resting-state or task-state. EEG, electroencephalogram; fNIRS, functional near infrared spectroscopy; qEEG, quantitative EEG; HD-EEG, high-density EEG; PSD, power spectrum density; PRI, power ratio index; BSI, brain symmetry index; PSI, phase synchrony index; FC, functional connectivity; TMS-EEG, transcranial magnetic stimulation combined with EEG; TEP, TMS-evoked potential; HbO, oxygenated hemoglobin; HbR, deoxygenated hemoglobin.

or alerting by thinking or calculating. Beta waves (13–30 Hz) reflect alertness and active concentration, which is generally regarded as normal rhythm in patients who are alert or anxious or have their eyes open. It may be reduced or absent in areas of cortical damage. Finally, gamma waves (30–150 Hz), the highest frequency band, arise from coordinated firing between neuronal populations during demanding cognitive and motor activities [11].

During EEG analysis, Delta and Theta waves were defined as low-frequency activity or slow-wave and Alpha, Beta, Gamma waves as high-frequency activity or fast-wave. PRI is defined as the ratio of power in slow-wave activity (delta and theta frequency bands) to that in fast-wave activity (alpha and beta frequency bands) [12] (Figure 1). In stroke, the increased slow activity and reduced Alpha frequency are always related to worse outcomes [13, 14]. An abnormal increase of Delta is usually associated with a primary brain injury, and Alpha relative power below 10 % is highly specific for a poor functional outcome [15]. However, the activation of Alpha indicates the survival of neurons in the stroke area and a good prognosis [16]. An increase of PRI has long been recognized following a recent stroke and associated with poor functional outcomes after stroke [17]. Besides, the delta-alpha ratio (DAR) is inversely correlated with functional outcomes, such as the Modified Rankin Scale (mRS) [14], Fugl-Meyer Assessment (FMA) [18], Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) [19, 20]. Therefore, after stroke, lower Alpha relative power, higher PRI or DAR are potential biomarkers to predict poor motor functional outcome.

Brain symmetry index (BSI)

The brainwave symmetry between hemispheres, quantified by the BSI, is another useful parameter to assess motor functional impairment during stroke assessment and rehabilitation. The BSI compares the power spectra between the two hemispheres and provides the magnitude of their asymmetry (Figure 1). This index, calculated as the mean absolute difference in hemispheric power spectra within the

1–25 Hz range (ranging from 0 for perfect symmetry to 1 for maximal asymmetry), was initially employed to detect early brain ischemia during carotid surgery but has gained wider application in evaluating ischemic changes and their impact on motor recovery following stroke.

Healthy individuals exhibit BSI values closer to 0, while higher values are indicative of stroke-related asymmetry. Van Putten et al. [21] confirmed a significant positive correlation between BSI scores and National Institutes of Health Stroke Scale (NIHSS) scores, suggesting that BSI can be used to monitor possible functional changes in such patients. Sebastián-Romagosa et al. [22] further revealed a close relationship between BSI and upper extremity motor function, as measured by FMA of Upper Extremity (FMA-UE) scores [23–26], while correlation with lower extremity function was not significant. The predictive power of BSI extends beyond initial assessment, with increased asymmetry linked to reduced survival odds in stroke patients [27]. A multitude of studies has investigated BSI's utility in predicting motor function across acute [28], subacute [22], and chronic [29] stroke phases. Consistently, higher BSI values have been associated with worse neurological status [21, 30] and weaker motor recovery at follow-up periods ranging from 2 months [27] to 6 months. These findings suggest BSI's potential as a negative predictor of motor function recovery after stroke. Agius Anastasi et al. [27] found that subacute stroke patients exhibited a significantly higher BSI compared with healthy controls, and early BSI significantly correlated with motor function later in recovery.

In addition to the standard BSI, various modified parameters derived from BSI, such as Directional BSI (BSIdir) and Pairwise Derived BSI (pdBSI), have been developed. These parameters, based on specific brain regions, enhance the sensitivity of BSI in analyzing EEG changes in stroke patients, and have demonstrated effectiveness in assessing clinical motor function states post-stroke [18]. For instance, stroke-induced alterations in slower background rhythms, particularly in the delta and theta bands, were observed through BSI analysis per frequency band. Chronic stroke survivors exhibited significantly more pronounced asymmetry, with the BSI in the delta and theta bands negatively associated with FMA-UE scores, indicating that greater asymmetry in these lower frequency bands correlated with more severe impairment [29]. BSIdir, accounting for the directional aspect of asymmetry, discerns whether the power is elevated in the left or right hemisphere [29]. In stroke survivors with more severe impairment, the hemisphere affected by the lesion exhibits heightened power, particularly in the delta and theta frequency band, compared to the unaffected hemisphere. Another metric, pdBSI, assesses asymmetry in PSD along homologous channel pairs, departing from the conventional global asymmetry approach. The physiologically grounded mathematical reformulation of the symmetry model enhances the accuracy in identifying abnormal asymmetry in patients with concurrent contralateral lesions. In a study by Sheorajpanday et al. [31], pdBSI and PRI were investigated for their predictive value regarding functional outcomes, including disability, dependency, and mortality at 6 months post-ischemic stroke. The findings revealed significant correlations between pdBSI, PRI, and established clinical assessments such as the mRS and NIHSS. Notably, pdBSI measured between 6 and 72 h after stroke onset, beyond the acute time window (<6 h), demonstrated correlations with functional outcomes at day 7 and month 6. This suggests that pdBSI reflects early neurological outcomes, potentially serving as an independent and preferable predictor of functional outcomes at the 6-month mark after ischemic stroke. Consequently, the utilization of BSI holds promise for diagnosing stroke-related motor function and for the continuous monitoring of cerebral activity during stroke rehabilitation.

Phase synchrony index (PSI)

In contrast to the focus of the BSI on power spectra asymmetry, the PSI, a qEEG measure derived from the phase of EEG, has emerged as a novel parameter for neural network analysis, representing synchronous brain activity [32] (Figure 1). Large-scale EEG synchrony abnormalities have been observed in various brain disorders, including stroke. Kawano et al. [32] assessed large-scale PSIs in stroke patients, specifically interhemispheric PSIs (IH-PSIs) in the alpha and beta bands, to analyze the association between IH-PSIs and FMA scores. The findings revealed no correlation between IH-PSIs and FMA scores. However, ipsilesional intrahemispheric PSIs (IntraH-PSIs) were correlated with Functional Independence Measure (FIM) scores, underscoring the utility of PSI in evaluating post-stroke motor impairment and recovery. In 2020, the same research team [33] revised the method to explore associations between IH-PSIs/IntraH-PSIs and the reduction of upper extremity motor impairment following rehabilitation. The results indicated that PSI (alpha band) between the primary motor cortex (M1) exhibited a selective correlation with FMA-UE scores. Additionally, the PSI (theta band) centered on the contralesional M1 selectively correlated with FMA-UE gain, with this correlation being particularly significant in severely impaired patients. These outcomes suggest that PSI has the potential to serve as a biomarker for evaluating both post-stroke motor impairment and recovery.

Functional connectivity (FC)

It is widely acknowledged that the brain functions as a highly intricate system, organized into a set of widely distributed functional networks. Following stroke, disruptions and reorganization of function are evident not only in the affected areas but also in the connected cortex [34]. The central question revolves around understanding how the recovery of function post-stroke is influenced by the brain's functional networks. Employing a connectivity-based approach to evaluate cortical reorganization underlying neurological deficits may uncover more profound mechanisms involved in functional network remodeling during rehabilitation. Functional interaction, a method rooted in measuring statistical dependencies among remote neurophysiological events based on correlations in measures of neuronal activity, is a typical approach for assessing FC [35]. The FC among different brain regions is posited to better capture the complexity of cortical processing, demonstrating a more robust association with behavior [36] (Figure 1). This connectivity shows the potential to serve as a predictive indicator for motor function outcomes and the efficacy of rehabilitation therapy.

FCs between the ipsilesional and contralesional hemispheres were reported to be correlated with motor function recovery. In a study by Wu et al. [23], resting-state connectivity measures were employed to assess their relationship with motor deficits across 28 days of intensive therapy targeting arm motor deficits. The findings indicated that connectivity between ipsilesional M1 and premotor cortex (PMC) increased concomitantly with motor gains, with larger increases in connectivity associated with greater motor improvement. This suggested that EEG measures of ipsilesional motor cortical connectivity are strongly linked to motor deficits and their amelioration, potentially serving as valuable biomarkers for cortical function and plasticity. Additionally, it was revealed that FCs between ipsilesional M1-PMC in the beta frequency band exhibited a negative correlation with upper limb functional recovery during a finger movement task [37]. Hoshino et al. [38] investigated FCs among EEG electrodes placed on bilateral motor-related areas to assess their predictive capability for upper limb motor function recovery in patients during the recovery stage post-stroke. The upper limb function was found to be correlated with FCs of EEG between M1 and PMC in the ipsilesional hemisphere. At 4 weeks post-stroke, intra-hemispheric FC exhibited reciprocal differences between ipsilesional and contralesional hemispheres. By 8 weeks, a significant correlation was identified between inter-cortical FCs in the beta band and the FMA-UE score, with FCs obtained at 4 weeks serving as predictors for the FMA-UE score at 8 weeks post-stroke. Subsequently, the same research group reported on the relationship between EEG signals during ankle movement and the lower extremity function measured by the FMA-LE score [39]. The results showed that higher intra-hemispheric FCs in both hemispheres, both in the resting state and during ankle movement at 4 weeks, were associated with improved lower limb function at 8 weeks. Hence, FCs in both upper and lower extremities closely reflect motor function recovery after stroke.

Despite numerous studies demonstrating the potential of EEG parameters like spectral power, symmetry indices, and connectivity metrics in forecasting post-stroke functional outcomes compared to clinical assessments or imaging biomarkers, the precise relationship between cerebral lesions and recovery remains multifaceted and enigmatic. Notably, direct comparisons of these EEG measures have produced inconsistent results, necessitating further, broader investigations [40]. Future research endeavors should explore potential correlations between these metrics and established outcome determinants, including age, infarct volume, and initial clinical severity, to elucidate a more comprehensive picture of post-stroke recovery and refine prognostication accuracy.

High-density EEG (HD-EEG)

The conventional EEG technique, employing the standard 10/20 EEG montage, offers high temporal resolution but a poor spatial resolution. Gel-based Ag/AgCl electrodes are used in EEG recording, with an electrolyte gel or paste facilitating optimal contact between the electrode and the scalp [41]. Knowledge of an individual's head anatomy and accurate positioning of EEG electrodes are essential for establishing realistic biophysical models [42]. However, the limited number of channels hinders the comprehensive evaluation of brain activity complexity and actual cortical FC [43]. Studies suggest that an inter-sensor distance of 1–2 cm can enhance the spatial resolution of EEG [44]. High-density 64-, 128- or 256-channel EEG (HD-EEG) provides excellent spatial resolution, allowing precise localization of cortical signal sources in real-time and assessment of whole-brain neuronal activity and functional network organization [3] (Figure 1). Besides, advances in saline-based leads and computational methods have further improved the resolution of HD-EEG for measuring task-related brain function [45].

Initially utilized in clinics to identify epileptic foci and address sleep pathophysiology, HD-EEG is now applied to evaluate motor functional status [45] and monitor patients' rehabilitation processes, aiding in understanding treatment effects and adjusting plans promptly [46]. Wu et al. [24] examined 3 min of resting-state EEG with HD-EEG (256 electrodes) in patients with acute ischemic stroke patients demonstrated a robust association between EEG data and NIHSS scores. HD-EEG data acquired acutely, hours to days after stroke onset, proved feasible as a bedside measure and strongly correlated with acute stroke behavioral deficits. Partial least squares (PLS) models were found to capture impairment better than traditional qEEG metrics, providing significant information about the injury not available from structural brain imaging. Mazurek et al. [25] employed a groundbreaking approach, combining 64-electrode EEG and motion capture systems, to delve into the intricate world of sensorimotor integration. This novel framework holds promise for identifying intact and damaged neural pathways in real-time, potentially revolutionizing stroke rehabilitation. By capturing the neural activity of the motor and parietal cortices using HD-EEG during rehearsal actions involving complex sensory manipulations, they demonstrated the power of this integrated approach in elucidating the impact of stroke on movement-related neural processing. Their findings highlight the impaired sensory-motor communication in stroke patients, laying the groundwork for developing neurorehabilitation systems that more effectively restore motor function by targeting these specific neural deficits [25]. Similarly, Iwama et al. [26] integrated neural feedback training with robotic devices for motor function assessment by employing HD-EEG to extract cortical motor excitability in real time. Patients can guide neural activity and consequently improve upper limb motor function through a closed-loop feedback system linking their brain activity with the robotic device and computer interface.

The alterations in both structural and functional coupling between hemispheres following stroke exhibit a correlation with the extent of motor injury and subsequent recovery. Hence, HD-EEG can serve as a predictive tool for functional outcomes post-stroke. Pichiorri et al. [47] devised an index of interhemispheric connectivity derived from HD-EEG, establishing an EEG-based measure that assesses interhemispheric cross-talk and aligns with functional motor impairment in subacute stroke patients. This EEG-based index enables the evaluation of the efficacy of training aimed at rebalancing hemispheres and, consequently, informs the development of future connectivity-driven rehabilitation interventions [47]. In a study by Nicolo et al. [48], HD-EEG data and standardized motor test results were recorded for 24 stroke patients at 2–3 weeks and 3 months post-stroke onset. The findings revealed that increased coherence of neural oscillations in motor areas with the rest of the cortex at 2–3 weeks post-stroke correlated with subsequent improvements in motor functions over the following weeks. The beta-band weighted node degree at the ipsilesional motor cortex exhibited a linear correlation with enhanced subsequent motor improvement. Clinical recovery was further associated with the contralesional theta-band weighted node degree. These correlations were specific to each corresponding brain area and independent of initial clinical severity, age, and lesion size. These observations underscore the utility of HD-EEG as a prognostic biomarker for motor function outcomes post-stroke.

Besides, HD-EEG is widely used in brain computer interface (BCI) systems. Pichiorri et al. [49] conducted an investigation about how sensorimotor rhythm-based BCI training induces persistent functional changes in the motor cortex. Using transcranial magnetic stimulation (TMS) and HD-EEG, they examined the functional alterations in the motor cortical system following motor imagery (MI)-based BCI training. The study confirmed that BCI control based on the motor cortex leads to changes in motor cortex excitability, evidenced by an enhancement in the representation of hand muscles. This increase in excitability was observed 24–48 h after training. In another study, Pichiorri et al. [50] explored cortico-muscular coherence (CMC) patterns derived from HD-EEG and electromyogram (EMG) for a rehabilitative hybrid BCI, achieving high classification performances in capturing motor abnormalities of stroke patients during simple hand movements. The analysis of CMC networks (derived from multiple HD-EEG and EMG channels) during simple hand tasks in stroke patients and healthy participants revealed that CMC network properties correlated with upper-limb motor impairment, as assessed by FMA and Manual Muscle Test in patients. These correlations with upper limb motor impairment support the use of CMC networks in a BCI-based rehabilitative approach. Vukelić et al. [51] assessed a neurofeedback training intervention involving modulating beta-activity in circumscribed sensorimotor regions through kinesthetic motor imagery. HD-EEG was employed to examine the reactivity of the cortical motor system during training sessions for right-handed healthy participants. The study involved visual feedback with a BCI and proprioceptive feedback with a brain-robot interface (BRI) orthosis attached to the right hand in a cross-over design. The results revealed that both feedback modalities activated a distributed FC network of coherent oscillations, uncovering a motor learning-related network and confirming the functionality of BCI and HD-EEG.

While HD-EEG offers enhanced spatial resolution for studying brain activity following stroke, it does not significantly enrich qualitative information compared to standard

EEG. Unfortunately, its primary challenge lies in data management. The substantial volume of data obtained, particularly with HD-EEG, necessitates substantial post-processing analysis to extract meaningful insights. Significant advancements in data analysis and interpretation are crucial before this technology can reach its full potential in clinical settings.

TMS combined with EEG, TMS-EEG

Besides spontaneous EEG, brain response to external stimulation may provide useful information about the brain network and function status after stroke. TMS, a form of non-invasive brain stimulation, can depolarize the cortical neurons induced electrical field and monosynaptic afferent, and the resulting activation may spread to connected brain regions. The distributed cortical response can be recorded with EEG. Combining TMS with real-time EEG recording may provide direct, immediate, and quantifiable measure of the local and throughout cortical response to TMS in individual patients [52] (Figure 1). TMS-EEG has significant potential for exploring the brain connectivity and recovery patterns for functional networks after stroke by measuring the cortical response to TMS which may be classified into TMS-evoked potentials (TEPs) and TMS-related cortical oscillations [53].

TMS-evoked potentials (TEPs)

TEPs, representing electrophysiological responses induced by TMS, are derived by isolating EEG responses that are phase-locked to the time of TMS application. These potentials mirror the direct activation of cortical neurons at the stimulation site, enabling the estimation of regional excitability in the motor cortex. Consequently, TEPs offer the potential to investigate the excitability and connectivity of the cortex in a causal manner, reflecting overall cortical reactivity across both motor and non-motor systems [54]. In contrast to the well-established TMS-induced motor evoked potential (MEP), which reflect the activity of descending corticospinal tracts (CST), TEPs provide additional insights into the integrity of cortical-subcortical pathways crucial for functional recovery after stroke [55]. Due to not relying on distal components like the spinal cord or peripheral nerves, TEPs can assess cortical reactivity even when the CST is severely compromised at subcortical levels [56]. Besides, TEPs can be obtained in individuals with stroke using lower stimulation intensities than those conventionally employed for recording MEPs. TEPs thus offer a unique opportunity to probe cortical physiology in this subset of stroke survivors. The combined assessment of MEPs and TEPs may contribute to a more comprehensive evaluation of the functional brain state.

TEPs are characterized by series of positive and negative waveforms with a duration of up to 300 ms. The TEPs peaks over M1 are N15, P30, N45, P60, N100, and P200 [55] (Figure 1). The frequency, amplitude, and area under the curve can be quantified to for its characters. These successive components delineate the propagation of activity from the stimulation site, furnishing information on the state of the brain network [56, 57]. The early peaks primarily reflect excitatory activity, with N45 potential reported to be mediated by gamma-aminobutyric acid (GABA)-A receptor activity and N100 potential by GABA-B receptor activity [57]. Numerous studies have associated the N100 component with cortical inhibitory processes [58]. In a study by Mangonatti et al. [59], the presence of the N100 component of TEPs in the lesioned M1 during acute stroke was identified as a predictor of favorable recovery, while the absence of N100 correlated with poor outcomes. Bai et al. [60] conducted concurrent TEPs measurements in chronic stroke patients, revealing that ipsilesional TMS produced a reduction in N100 amplitude around the stimulated M1, significantly correlated with changes in ipsilesional MEP. Hoedacre et al. [61] recorded TEPs with HD-EEG in chronic stroke survivors performing a motor function task utilizing a customized grip-lift manipulandum. They observed a larger amplitude and delayed latency of the P30 component in chronic stroke patients, suggesting its potential use as a biomarker for upper-limb behavior.

It is now understood that TEPs exhibit propagation to the contralateral side and other interconnected brain regions through corticocortical fibers or subcortical structures. Analyzing the latencies and cortical distribution enables the inference of activity propagation from the stimulation site to anatomically connected ipsilateral or contralateral regions. This analysis provides valuable insights into the connectivity of different cerebral cortex areas [62]. In a study by Ding et al. [63], TEPs recorded with EEG were utilized to investigate neurophysiological changes post-stroke and their association with behavioral changes. The results showed that the FC was increased gradually in individuals even without elicitable MEP during stroke recovery. TEPs can also serve as a tool to investigate interhemispheric FC in stroke patients. Casula et al. [64] observed that TMS applied over the contralesional M1 induced suppression of activity in the lesioned hemisphere. Patients exhibiting a more balanced TEPs pattern between hemispheres demonstrated better functional recovery, confirming that an imbalance in interhemispheric inhibition exacerbates motor dysfunction in stroke patients.

TMS-evoked oscillation

The TMS-evoked EEG response can also undergo analysis in the time-frequency domain, where the stimulated region may generate or entrain oscillations in discrete frequency bands [65]. These oscillatory patterns can be categorized into frequency bands based on physiological properties, spanning from delta to gamma [66]. Such frequency band analysis can be employed to examine FC in the cortex. Higher cortical reactivity, characterized by faster and more complex evoked oscillatory activity in lesioned motor areas, reliably indicates favorable motor recovery after stroke [67]. Pellicciari et al. [67] established the initial connection between TMS-evoked alpha activity and motor function. They monitored TMS-evoked oscillations in different frequency bands in subcortical stroke patients and found that baseline TMS-evoked alpha oscillatory activity was associated with improved functional recovery at 40- and 60-day follow-up assessments. This suggests that the intensity of the alpha rhythm can be considered a reliable predictor of motor recovery [67]. In a study by Tscherpel et al. [68], the relationship between TMS-evoked EEG activity and motor recovery 3 months post-stroke was examined. They found that in the early phase post-stroke, the significant alterations in low-frequency oscillations of ipsilesional M1 and less deflections were associated with more pronounced motor impairment. And a positive correlation between the numbers of deflections of the EEG response and motor recovery outcome was also found. This implies that TMS-EEG may provide distinct response patterns, indicating the individual potential for functional recovery.

In summary, TMS-EEG emerges as a potent tool for studying post-stroke motor functional recovery. Its ability to capture motor-related cortical activity, oscillatory events, and brain FC, irrespective of CST integrity, enables investigation of the underlying neural mechanisms from diverse perspectives.

fNIRS for motor function assessment and rehabilitation after stroke

FNIRS is a novel functional neuroimaging modality that utilizes paired optodes of near-infrared light emitters and detectors separated by 3–4 cm. These optodes can be strategically positioned across various areas on the scalp to estimate changes in the concentration of both oxygenated (HbO) and deoxygenated (HbR) hemoglobin based on the modified Beer–Lambert law [69]. Following the neurovascular coupling theory, alterations in hemoglobin concentrations signify increases in cortical brain activation [70]. With a recording depth of 1.5–2 cm, fNIRS reaches the cortical layer of the cerebral cortex, offering a relatively high spatial resolution compared to EEG, which can identify source activity to a certain extent. Due to its portability, silent measurement nature, and low sensitivity to motion artifacts, fNIRS is considered a promising tool for investigating potential neuroplastic changes associated with motor functional rehabilitation interventions in stroke patients, particularly during movement activities like walking [71]. Common applications of fNIRS in post-stroke motor function include monitoring FC during rehabilitation treatments and predicting outcomes [69].

fNIRS in resting-state assessment of motor-related cortical activity and brain network after stroke

Due to the challenges faced by many post-stroke patients in performing tasks, resting-state FC (rsFC) analysis has become a common approach to study brain networks (Figure 1). In the resting state, fNIRS has been utilized to investigate the FC between brain regions, demonstrating comparable results to fMRI. By using fNIRS, Arun et al. [72] identified the FC patterns in stroke patients with upper limb deficits and their changes during the recovery phase. In a study involving 20 mild stroke patients within 4–8 weeks of onset, they observed disrupted ipsilateral connectivity and increased contralateral connectivity in left-hemisphere stroke patients. The connections between M1, somatosensory area, and PMC in the ipsilateral hemisphere improved after upper limb function recovery, suggesting that rsFC changes during recovery could predict the extent of motor deficit recovery. Similarly, Song et al. [73] investigated rsFC in the sensorimotor cortex using fNIRS on 73 participants: left hemiplegia (LH) patients, right hemiplegia (RH) patients, and healthy controls, within 1–4 months post-stroke. In healthy controls, M1 and M2 in the left hemisphere exhibited stronger rsFC compared to the right, revealing a typical asymmetry. However, this pattern was disrupted after stroke. Notably, RH patients, unlike LH ones, displayed a stronger rsFC between left primary sensory cortex (S1) and M1 compared to healthy controls, which inversely correlated with motor function. Within M1, a negative correlation was observed between rsFC in the ipsilesional hemisphere and motor function of the affected limb. Additionally, rsFC within the contralesional M1 innervating the unaffected limb was weakened compared to healthy controls. These findings suggest potential implications for TMS modulation of cortical excitability to promote plasticity. Besides, Wang et al. [74] compared resting-state prefrontal cortex (PFC) oxygenation levels in 17 stroke patients with limb motor dysfunction and 9 healthy controls using fNIRS. Prefrontal HbO concentration was significantly lower in stroke patients, and the PFC lateralization index positively correlated with the FMA score. This suggests that stroke induces cerebral hemodynamic changes in the PFC, and fNIRS-derived hemodynamic activity can serve as a reliable neurobiomarker for assessing limb motor dysfunction in stroke patients.

Therefore, the rsFC measurement using fNIRS can effectively discern alterations in the motor cortical network during the recovery of motor function. The notable advantage lies in the effortless nature of this approach for stroke patients, as it does not entail specific tasks during the measurement paradigm. Looking ahead, the integration of machine learning algorithms with rsFC data holds potential for predicting recovery from stroke based on the rehabilitation strategy employed, utilizing information gleaned from rsFC measures of the patients.

fNIRS in task-state assessment of motor-related cortical activity and brain network after stroke

The foremost advantage of fNIRS lies in its suitability for real-time monitoring of brain activity during exercise, owing to its portability and patient-friendly features. Over the past few decades, methodological and technological advancements have propelled the utilization of fNIRS in assessing motor function. Initially employed for single 'point' measurements during basic motor tasks (e.g., finger opposition, finger tapping), it has evolved to support multichannel topographic mapping of more intricate motor paradigms (e.g., pursuit rotor tasks, walking). Studies have demonstrated the reliability of fNIRS in detecting changes in task-related responses after stroke and during the recovery period. For instance, fNIRS results have corroborated findings such as impaired contralateral M1 activations, up-regulation of ipsilateral motor activations, and longitudinal improvements in laterality towards contralateral M1 activation following rehabilitation [75]. Xu et al. [76] used fNIRS to study the brain activation and network patterns of upper limb isokinetic muscle strength training in subacute stroke patients. The study revealed that unilateral limb training significantly enhanced FC in the ipsilateral M1 and bilateral PFC compared to bilateral training. This study indicated that unilateral upper limb training may more effectively promote interaction and balance between bilateral motor hemispheres, contributing to brain reorganization in the ipsilateral M1 and PFC in stroke patients.

FNIRS can provide information of motor-related brain network in various stages of stroke. Lim et al. [77] utilized fNIRS to observe the activation of the sensorimotor cortex in 11 chronic stroke patients during a reaching and grasping task. Despite poorer performance on the grasping task in the stroke patients, the results revealed greater ipsilateral hemispheric sensorimotor activation in the stroke group in both reaching and grasping conditions compared to healthy controls. Significant correlations between gripping performance and sensorimotor activation were observed exclusively in the stroke group, highlighting the potential of fNIRS in assessing differences in brain activation during functional positional movements after stroke. Huo et al. [78] applied fNIRS to evaluate cortical responses in subacute stroke patients (onset <180 days) during upper limb task-oriented training and cyclic rotation training. The outcomes demonstrated that task-oriented training significantly increased activation in both hemispheres and enhanced prefrontal influence on the motor cortex compared to cyclic rotation training. Task-oriented training involved widespread contralateral hemisphere activation. This study validates the feasibility of combining fNIRS with motor paradigms to assess real-time neural responses associated with stroke rehabilitation. In another study, Huo et al. [79] investigated the impact of repetitive TMS (rTMS) combined with bilateral arm training (BAT) on brain functional reorganization in chronic stroke patients using fNIRS. The results showed that the differences of FC responses in stroke patients treated with unilateral arm training alone or with rTMS-BAT were more pronounced than in healthy controls. In the resting state, stroke patients exhibited significantly lower FC than controls in both hemispheres. Following rTMS-BAT, the clustering coefficient and local efficiency of the contralateral M1 in stroke patients were significantly reduced, while the local efficiency of the ipsilateral M1 was significantly increased. Moreover, these two network indicators were significantly positively correlated with motor function in stroke patients. This study suggests that fNIRS-based assessments offer valuable insights into the neural mechanisms underlying combination interventions for stroke rehabilitation.

Task-related fNIRS holds promise for assessing dynamic brain activation and network reorganization during various interventions, enhancing the precision of rehabilitation strategies and ultimately contributing to more effective motor recovery after stroke. Employing a wireless and portable fNIRS device, Lim et al. [80] measured the functional brain activity when the participants performed walking trials along a 50-m hallway. The study revealed sustained activation in the PFC, with greater activation in the ipsilesional hemisphere. The sensorimotor cortex exhibited activity primarily during the early acceleration stage of walking, while the posterior parietal cortex showed changes in activation during the later steady-state stage. Moreover, faster gait speeds were associated with increased activation in the contralesional sensorimotor and posterior parietal cortices. This underscores the significance of the prefrontal, sensorimotor, and posterior parietal cortices in post-stroke walking, with individuals exhibiting greater fNIRS activation tending to achieve better physical outcomes. Lu et al. [81] utilized fNIRS to investigate brain network patterns in 18 stroke patients during four-limb linkage rehabilitation training. The study findings indicated a decrease in FC at 0.052–0.145 Hz and 0.021–0.052 Hz in stroke patients compared with healthy controls, suggesting disturbed neurovascular coupling regulation due to brain impairments. Notably, significant differences in wavelet phase values (akin to global connectivity) between right-hemisphere and left-hemisphere stroke patients during rehabilitation training highlighted the need for task-specific rehabilitation design tailored to individual needs. This study suggests that frequency-specific FC methods offer a potential approach for quantitatively assessing the effectiveness of rehabilitation tasks.

Nevertheless, a notable limitation inherent to fNIRS is its measurement of cortical activation without providing precisely anatomical information about the specific region being examined. Therefore, ensuring the reliability of optode placement over the targeted cortical region is crucial. This is particularly pertinent in longitudinal studies of motor skill acquisition where consistent optode placement between sessions is paramount for repeatedly probing the same cortical region [75].

Integration of fNIRS-EEG for motor function assessment after stroke

Cortical reorganization during post-stroke treatment is generally related to regional excitability as well as abnormal connections between relevant function areas. As previously discussed, fNIRS captures changes in hemoglobin oxygenation in the brain cortex, while EEG records the brain's electrical activity. To be specific, in addition to generating electrical signals to be detected by EEG, neuronal activity is also accompanied by changes in cerebral blood flow. When neurons are activated, the brain region where neurons are located will have an increase in cerebral blood flow, causing changes in HBO and HBR concentrations, which can be detected by fNIRS [82]. Combining the two modalities in a multi-modal approach known as fNIRS-EEG can not only be used to explore the dynamic alteration of cortical excitability and connectivity after stroke, but also probe into the correlation between neuronal changes and neurovascular coupling, and increase the accuracy of functional localization of the brain under specific tasks or conditions. Showing great potential for understanding the relationship between dysfunctional brain network and motor impairment. The studies regarding fNIRS-EEG application in motor function after stroke are shown in Table 1.

Theoretical and technical basis of fNIRS-EEG

EEG can more accurately, continuously, and dynamically monitor the brain activity of stroke patients. fNIRS uses near-infrared light, while EEG uses electrical signals. Therefore, these two technologies are complementary in principle, do not interfere with each other, and can provide a wealth of information for brain function assessment. As a complement to EEG source localization, fNIRS is more suitable for studying brain activity related to human movement control in real-life situations (such as sitting or standing). Li et al. [83] and others have demonstrated the feasibility of using fNIRS-EEG to monitor and predict motor recovery in stroke patients. The multimodal detection of fNIRS-EEG can overcome the limitations of poor portability and low temporal resolution of fMRI, providing more comprehensive and accurate information for monitoring, assessing, and predicting motor function recovery in stroke patients.

The integration of fNIRS and EEG requires hardware synchronization. That is to say, to achieve precise registration of fNIRS and EEG data, the data collection hardware of both systems must be synchronized. Uchitel et al. reviewed some of the progress in hardware coupling between fNIRS and EEG over the last decade or so, which includes following approaches [84]. In 2013, Safaie et al. integrated EEG and fNIRS components using a custom-designed optoelectronic "patch" [85]. In 2017, von Luhmann et al. developed an integrated multichannel fNIRS-EEG system, in which a 24 bit analog-to-digital converte is used for both fNIRS and EEG data acquisition [86]. In 2019, Lee et al. proposed an integrated system of fNIRS-EEG based on dry electrodes. The system incorporates 8 fNIRS channels and 16 dry electrode EEG channels [87]. The two detection methods of fNIRS and EEG are complementary in information. The information of cerebral blood oxygen level provided by fNIRS is related to

Table 1: Summary of fNIRS-EEG fusion studies.

Conclusions	FNIRS-EEG brain activation patterns as a marker of underlying residual function that correlate with the functional outcome and/or performance may be facilitated with individualized brain-state dependent tDCS during neurorehabilitation	portable NIRS-EEG joint imaging can be incorporated into brain computer interfaces to monitor tDCS-facilitated neurointervention as well as cortical reorganization	The proposed multimodal EEG/fNIRS technique demonstrates a preliminary potential for monitoring and predicting poststroke motor recovery	Multimodal EEG/fNIRS technology has shown initial potential for monitoring and predicting motor recovery after stroke	ERD and HBO during ankle dorsiflexion and age were promising biomarkers for stroke motor recovery
Outcomes	1. Post-tDCS changes in the mean rSO_2 from baseline mostly correlated with the corresponding post-tDCS change in log-transformed mean-power of EEG within 0.5–11.25 Hz. 2. A decrease in log-transformed mean power of EEG within 0.5–11.25 Hz corresponded with an increase in the MEP-measure of corticospinal excitability	For the contralesional hemisphere, a strong positive correlation between intrinsic mode functions of regional cerebral hemoglobin oxygen saturation and the log-transformed mean-power time-series of intrinsic mode functions for EEG with a lag of about −15 s was found after a cumulative 550 s stimulation of anodal tDCS	1. The task-evoked strength at ipsilesional S1 was significantly lower in stroke patients compared with healthy controls. 2. Across the 4-week rehabilitation intervention, the strength at ipsilesional PMC and the connectivity between bilateral M1 increased in parallel with the improvement of motor function. 3. A higher baseline strength at ipsilesional PMC was associated with a better motor function recovery, while a higher baseline connectivity between ipsilesional SMA–M1 implied a worse motor function recovery	1. The modal controllability of ECN in stroke patients was significantly lower than healthy subjects. 2. The modal controllability of SMA in stroke patients was also significant smaller than healthy subjects. 3. The baseline modal controllability of M1 was found to be significantly correlated with the baseline FM-UL clinical scores	ERD, HBO, PSI, and age were critical biomarkers in predicting Berg Balance Scale
Software	StimViewer, Neuroelectrics, Spain;Matlab, EEGLAB	SimNIBS; MoBILAB toolbox; AtlasViewer software; OpenMEEG toolbox; AtlasViewer; Matlab, EEGLAB	Matlab, EEGLAB;Freesurfer	Matlab, EEGLAB	Matlab, EEGLAB;The oxygenation monitor software
Hardware(fNIRS)	INVOS Cerebral Oximeter Model 4100, USA;SomaSensor (SAFB-SM, INVOS, USA)	SomaSensor (SAFB-SM, INVOS, USA)	NIRScout, NIRx Medizintechnik GmbH	NIRScout, NIRx Medizintechnik GmbH	NirScan, Danyang Huichuang Medical Equipment Co., Ltd.
Hardware(EEG)	StarStim, Neuroelectrics, Spain	StarStim, Neuroelectrics, Spain	Brain Products GmbH	Brain Products GmbH, Germany	Neuroscan, Victoria, Australia
Methods	Using fNIRS-EEG joint-imaging during and after anodal tDCS to measure changes in mean rSO_2 along with changes in the log-transformed mean-power of EEG within 0.5–11.25 Hz	EEG was used to measure neural activity and fNIRS was used to measure the hemodynamics of NVC to simulate the NVC of lesion and contralateral hemisphere in patients with ischemic stroke	EEG-fNIRS data were simultaneously recorded from 9 healthy controls and 18 stroke patients during a hand-clenching task. A novel fNIRS--informed EEG source imaging approach was developed to estimate cortical activity and functional connectivity. Subsequently, graph theory analysis was performed to identify network features for monitoring and	FNIRS-EEG were simultaneously recorded from 16 stroke patients and 11 healthy subjects during a hand-clenching task. A high spatiotemporal resolution fNIRSinformed EEG source imaging approach was then employed to estimate the cortical activity and construct the functional brain network. Subsequently, network	Extracting the ERD, HBO and PSI features during ankle dorsiflexion from fNIRS-EEG. Builting a linear regression model predicting BBS values and tested the model using 8-fold cross-validation

Table 1: (continued)

			predicting motor function recovery during a 4-week intervention	control theory was applied to evaluate the modal controllability of some key motor regions, including M1, PMC, and SMA, and also the ECN	
Authors (Years)	Jindal U, et al. (2015)	Guhathakurta D, et al. (2016)	Li R, et al. (2020)	Li X, et al. (2022)	Liang J, et al. (2022)
Title	Corticospinal excitability changes to anodal tDCS elucidated with fNIRS-EEG joint-imaging: An ischemic stroke study	Computational Pipeline for fNIRS-EEG Joint Imaging of tDCS-Evoked Cerebral Responses-An Application in Ischemic Stroke	Multimodal Neuroimaging Using Concurrent EEG/ fNIRS for Poststroke Recovery Assessment: An Exploratory Study	Functional Brain Controllability Alterations in Stroke. Front Bioeng Biotechnol	Prediction of balance function for stroke based on EEG and fNIRS features during ankle dorsiflexion

neuronal activity, while the information of cerebral electrical signal provided by electroencephalogram is related to neuronal discharge. By combining fNIRS with EEG, more accurate and comprehensive neural network information can be obtained. In order to achieve accurate registration of fNIRS and EEG data and obtain reliable research results, it is necessary to ensure the synchronization of data recording of the two technologies. Synchronous recording ensures proper alignment of fNIRS and EEG data, which is critical for subsequent processing. This can be done by using a common trigger signal or by time-stamping data from both systems.

This integration enables the exploration of correlations between neuronal changes and neurovascular coupling (Figure 2). Combined application can mitigate some of the limitations inherent in each modality [88], yielding heightened sensitivity and specificity. A limitation of EEG is the volume conduction problem. A single electrode on the scalp picks up activity from numerous sources (cortical activity, cortical activity, external noise, etc.), which leads to difficulty in accurately locating the source activity. Moreover, the accuracy of current EEG-based source localization techniques to localize subcortical activity is still controversial [89]. Given the high spatial resolution of fNIRS, fNIRS-informed EEG source is a deep fusion of fNIRS and EEG signals. A study by Li et al. showed that fNIRS was used as a reliable reference for choosing the most representative task-related EEG channels for analysis, which optimized the analysis strategy of EEG [82]. Therefore, fNIRS-informed EEG source not only can improve the low spatial resolution of single EEG, but also make up for the lack of temporal resolution of single fNIRS and increase the ability to detect activity in deeper brain structures. By obtaining measurements from both modalities, it becomes feasible to obtain complementary information regarding the functional activity of the brain without encountering electro-optical interference [82]. This synergistic approach holds the potential to refine the characterization of neural network functional activities with greater precision. Moreover, fNIRS and EEG signals are inherently linked to neuron metabolism-hemodynamics and neuronal electrical activity, respectively, providing built-in validation for the identified activity. The fNIRS-EEG system leverages the strengths of both technologies, offering high mobility, non-invasiveness, and cost-effectiveness. This combined data collection can be conducted in non-laboratory settings without causing significant discomfort to subjects. Consequently, the multi-modal integration of fNIRS-EEG holds promise for introducing novel perspectives in the assessment of stroke motor function rehabilitation.

It is regrettable that the combination of fNIRS and EEG inevitably retains some of the limitations of each. For example, low sensitivity to motion artifacts is an advantageous feature of fNIRS; however, due to the inherent nature of EEG signal acquisition, this advantage is limited when fNIRS is used in combination with EEG. On the other hand, EEG is sensitive to magnetic interference, and the combination of fNIRS-EEG inherits this shortcoming. In addition, because the inherent response times of fNIRS and EEG are different, the parallel processing and temporal synchronization of fNIRS and EEG is an important issue [90]. Guhathakurta et al. measured the tDCS-induced response to stroke patients by fNIRS-EEG joint imaging, using a method based on Empirical Mode Decomposition of fNIRS and EEG time series to decompose into a set of intrinsic mode functions (IMF), and then conducted a cross-correlation analysis on those IMFs from fNIRS and EEG signals. It was found that there was a strong positive correlation between the

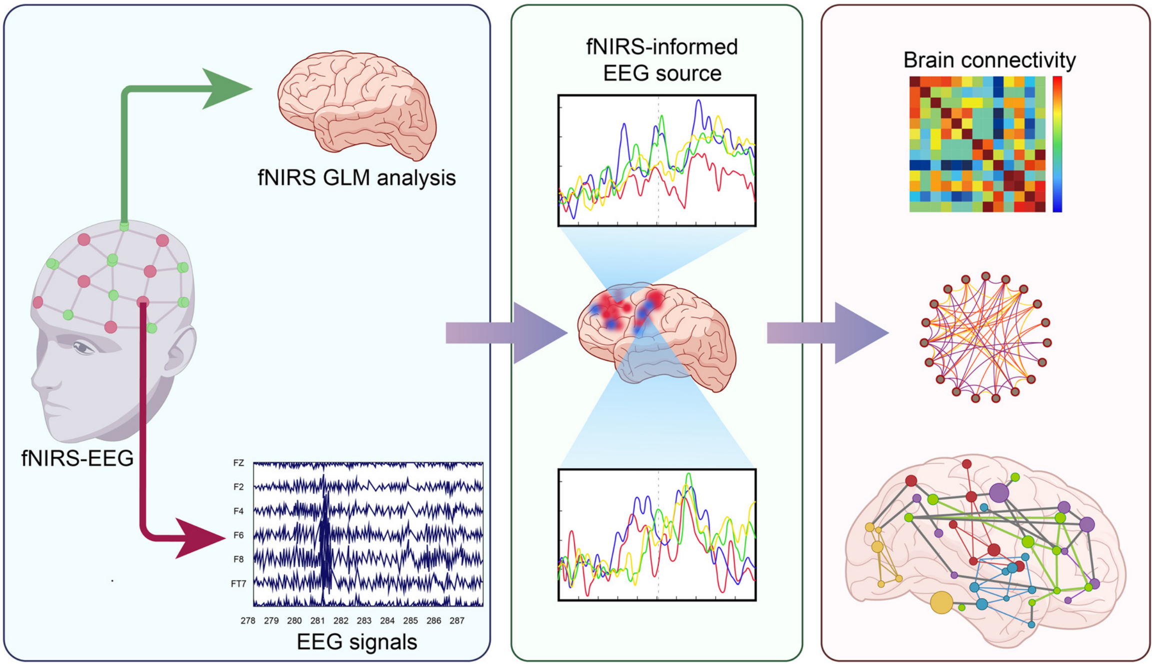

Figure 2: Integration of fNIRS-EEG for motor function assessment and rehabilitation after stroke. FNIRS data is analyzed (for example by GLM method). EEG signals analyses use a sliding window scheme. FNIRS informed-EEG source localization is used to investigate the brain connectivity, brain network dynamic process and the brain controllability analysis. GLM, general linear model.

logarithmic conversion average power time series of EEG IMFs and the IMFs with local cerebral hemoglobin oxygen saturation lag of about 15 s [91]. We expect that in the future, with the advancement of technology, these limitations can be well addressed.

Assessment of brain activity patterns

FNIRS-EEG can effectively map changes in brain activity after stroke, study the variations in neurovascular coupling during and after stroke, and aid in the comprehensive assessment of neurological deficits in stroke patients. Assessing the brain activity patterns of stroke patients through fNIRS-EEG not only reveals the neurobiological mechanisms of brain function recovery but also serves as an auxiliary assessment tool for rehabilitation outcomes. A study based on methods for evaluating neurovascular coupling (NVC) during fNIRS-EEG and anodic transcranial direct current stimulation (tDCS) found that the initial decrease in HbO2 at the beginning of anodic tDCS corresponds to an increase in the logarithmic transform average power of EEG in the band 0.50–11.25 Hz [92]. Similarly, Jindal et al. [93] used fNIRS-EEG to assess the changes of average cerebral hemoglobin oxygen saturation (rSO2) along with changes in the log-transformed mean-power of EEG within 0.50–11.25 Hz during tDCS treatment. The results show that the post-tDCS changes in the mean rSO2 from baseline mostly negatively correlated with the corresponding post-tDCS change in log-transformed mean-power of EEG within 0.50–11.25 Hz. And the decrease in log-transformed mean power of EEG within 0.50–11.25 Hz after tDCS intervention corresponds to the increase of MEP measurement of corticospinal excitability. These studies further expand the applications of fNIRS-EEG in evaluating brain activity patterns in stroke patients and assisting in quantifying the effects of tDCS intervention.

Assessment of FC

As mentioned above, FC serves as a crucial indicator of the interplay between different brain regions, reflecting changes in the brain post-stroke and indicating motor function recovery. In a study by Li et al. [83], fNIRS-EEG was employed to analyze cerebral cortical activity and FC in 18 stroke patients undergoing rehabilitation during the hand-clenching task. The fNIRS results revealed a significant reduction in blood oxygen-evoked intensity in the ipsilateral S1 of stroke patients compared to healthy controls. Concurrently, EEG results demonstrated an increase in beta frequency in the ipsilateral M1 and enhanced connectivity between bilateral M1 in correlation with improved motor function. In addition, higher baseline strength of ipsilateral PMC is related to better motor function recovery, while higher baseline connectivity between ipsilateral supplementary motor cortex (SMA)-M1 means poor motor function recovery. This research underscores the utility of multimodal fNIRS-EEG technology in evaluating brain FC to reflect motor recovery following stroke.

Brain functional controllability analysis in stroke

Brain functional controllability analysis, rooted in controllability theory, is a brain network analysis approach aimed at characterizing the capability of specific brain regions to regulate changes in brain behavior from one state to another, known as modal controllability of brain regions [94]. Li et al. [95] utilized fNIRS-EEG to assess the cortical activity of 16 stroke patients during a grasping task, enabling the calculation of modal controllability in motor-related brain areas. The findings indicated a significant reduction in modal controllability within the motor executive control network and SMA in stroke patients compared to healthy individuals. Moreover, the modal controllability of the M1 exhibited a significant positive correlation with upper limb motor function scores. This study underscores the potential of analyzing modal controllability in brain regions to unveil the neural mechanisms underlying motor control disorders in stroke patients, offering insights for rehabilitation treatments.

Prediction of stroke motor function outcome

The integrated use of fNIRS-EEG is valuable in predicting functional outcomes by analyzing brain activity data during the early stages of rehabilitation. Li et al. [83] introduced an algorithm based on fNIRS-EEG for assessing cortical reorganization after post-stroke. Through the combined application of fNIRS-EEG, both spatial and temporal course information of brain activity could be extracted simultaneously, leading to a more accurate assessment of brain FC in stroke patients. The study noted that FC in the ipsilesional SMA-M1 at baseline can predict the degree of functional improvement, with lower in the former and greater in the latter. This offers robust support for predicting and monitoring motor function functional recovery after post-stroke. In another study by Liang et al. [96], the prediction of balance function in stroke patients was explored through EEG parameter such as event-related desynchronization (ERD) and fNIRS parameter oxygenated hemoglobin. This study demonstrated highly correlated parameters, including ERD, PSI, and oxygenated hemoglobin, with berg balance scale values, suggesting these parameters as potential biomarkers for predicting stroke motor recovery. This study offered a new idea for guiding the rehabilitation of stroke patients, evaluating and predicting their recovery status.

Application in novel motor function rehabilitation approach for stroke

Application in optimizing tDCS treatment to improve motor function

As a non-invasive brain stimulation technique, tDCS entails the application of low-intensity direct current to the scalp to modulate the excitability of the central nervous system [97]. It induces changes in regional cerebral blood flow, with anodal tDCS leading to an increase in resting-state regional cerebral blood flow, while cathodal tDCS results in a decrease [98]. Consequently, tDCS has proven effective in facilitating motor function rehabilitation in the early stages of stroke [99]. However, the therapeutic efficacy varies due to the heterogeneity of the affected region. Therefore, enhancing the effectiveness of tDCS intervention based on the individual cerebral condition of the patient becomes imperative. By integrating fNIRS and EEG signals, the methodology enables the evaluation of neural and hemodynamic reactions in ischemic cerebral areas, potentially offering spatiotemporal characteristics for enhanced comprehension of the impact of tDCS on brain region responses after stroke, thereby predicting the probability of functional recuperation. For example, Guhathakurta et al. [91] employed a computational pipeline for portable fNIRS-EEG joint imaging to visualize the spatiotemporal discriminatory features of ischemia under tDCS and monitor tDCS-facilitated neurointervention as well as cortical reorganization. Moreover, the integration of fNIRS-EEG joint imaging technology also allows for the monitoring of changes in corticospinal excitability. This capability facilitates the customization of tDCS dosage for closed-loop control, leading to further improvements in cerebral function in cerebrovascular occlusive disorders [100, 101]. Additionally, the brain activation pattern identified through fNIRS-EEG, serving as an indicator of potential residual function linked to functional outcome and/or performance, can be utilized to enhance brain function restoration through personalized tDCS in the context of neurological rehabilitation. Dagar et al. [102] introduced the brain "excitation-inhibition balance" hypothesis, which posits that the equilibrium state of brain excitation is disrupted following brain injury. FNIRS-EEG was employed to assess the hemodynamics and neural activity potentials, thereby capturing the excitatory and inhibitory regions of the brain in stroke patients. By considering the excitatory and inhibitory states observed in healthy individuals, administering appropriate electrical stimulation parameters to stroke patients has the potential to enhance the impact of tDCS on motor function rehabilitation.

Application in BCI training on motor function after stroke

The evaluation of the impact of fNIRS-EEG on brain motor function activation serves as a valuable parameter for monitoring and regulating BCI technology during intervention training. Previous research has shown that MI primarily activates sensorimotor regions involved in physical task execution, and consistent MI practice induces neuroplastic changes. EEG has been the predominant modality for assessing BCI functionality, while studies exploring physiological signals from fNIRS provide deeper insights into brain activation states and physiological alterations [103, 104]. Integrating EEG and fNIRS signal characteristics has demonstrated the potential to improve the accuracy of MI classification. The effectiveness of multimodal fNIRS-EEG technology in monitoring and predicting motor recovery after stroke has been substantiated [83]. Wang et al. [105] used Functional Electrical Stimulation (FES) to stimulate distal muscles in stroke patients, coupled with BCI incorporating MI training feedback to quantify the impact on brain motor function activation. Results indicated that FES treatment with BCI feedback led to significant improvements in muscle strength and activities of daily living compared to the control group. Patients also exhibited enhanced levels of brain ERD, Event-Related Synchronization (ERS), and blood oxygen activation. This suggests that the fNIRS-EEG assessment is a valuable tool for monitoring brain responses during motor function rehabilitation training for stroke patients.

In summary, fNIRS-EEG has gained significant prominence in post-stroke motor function rehabilitation by combining electrical and optical measurements. This innovative approach enables the assessment of cerebral cortex activation levels and the connectivity of associated cortical functional networks. It also allows for the identification of additional features of brain activation and connectivity, enhancing the comprehensive understanding of the neurophysiological mechanisms underlying motor behavior impairment and neurological disorders. The incorporation of a precise and quantitative feedback mechanism has the potential to improve the efficacy and clinical utilization of post-stroke rehabilitation treatments such as tDCS and BCI training.

Conclusions and future prospects

The heterogeneity of stroke pathology and recovery patterns makes it difficult to standardize the therapies. Accurately characterizing brain injury and brain function post-stroke could significantly impact clinical decision-making regarding therapy. EEG recording, a non-invasive technique available in most general hospitals, is widely used for monitoring motor function states and predicting outcomes after stroke. FNIRS is an emerging optical technique monitoring the activities of the brain by measuring the hemodynamic condition. It stands out for its size, weight, and real-time monitoring capabilities compared to other neuroimaging techniques. Applied to stroke patients, fNIRS monitors hemodynamic conditions during pre-, peri-, and post-motor rehabilitation, providing crucial insights into brain network damage, remodeling, and reorganization.

To gain a comprehensive understanding of the neurobiological and neurophysiological mechanisms behind changes in motor-related brain activation patterns, it is crucial to combine functional imaging techniques with high temporal and spatial resolutions, such as EEG and fNIRS. Integrating EEG with fNIRS offers multidimensional evidence and deeper insights into plasticity changes, with additional spatial details from hemodynamics and motor pathway physiology. However, the combined fNIRS-EEG technique exhibits several limitations which need to be overcome in the future. Firstly, placing optodes and electrodes in areas with significant variation in neuronal electrical signals and hemodynamics poses a scientific challenge. It is challenging to record neuronal electrical and hemodynamic activity from the same location. Many optodes are needed to cover the area of interest, which may be limited by scalp space when applying EEG with fNIRS. Advanced hardware development and integration of fNIRS optodes and EEG electrodes are necessary [69]. Secondly, data analysis is crucial for extracting effective parameters. The data may include directly measured signals, derived values, or a combination of fNIRS and EEG recordings. How to integrate the direct and indirect parameters and correlate them with conventional features for detecting motor function requires further large-scale investigation.

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